Progress report on the cost-effectiveness of X-linked adrenoleukodystrophy newborn screening

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X-ALD NBS Background

X-linked adrenoleukodystrophy (X-ALD) is a genetic disorder affecting one in 17,000 newborns and is caused by a mutation in the *ABCD1* gene. Although no symptoms are shown in newborns, X-ALD phenotypically manifests itself in children and adults in three main ways: cerebral ALD (cALD), abnormal adrenal function, and adrenomyeloneuropathy (AMN). cALD affects 35-40% of young male patients and results in a progressive deterioration of cognitive ability, vision, hearing, and motor function. Untreated, it leads to vegetative state followed by death. Abnormal adrenal function affects almost all males and usually presents within the first decade of life. Finally, AMN affects 40-45% of all patients with typical onset in the fourth decade of life. Although not life threatening, AMN results in stiffness and tingling in feet, difficulty walking, and issues with balance and strength.

X-ALD newborn screening is hypothesized to lead to significantly earlier diagnosis for patients affected by cALD and abnormal adrenal function—translating to dramatically improved survival and markedly reduced morbidity.

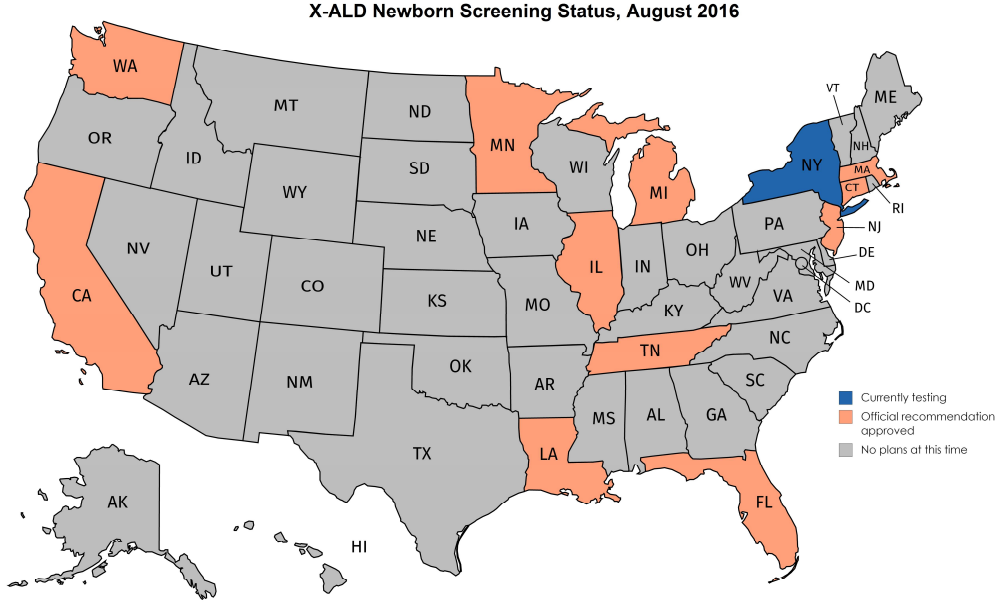
Markov Model Background

Markov models seek to outline all the possible states of a system and the transition paths between those states. Within the context of X-ALD, the possible states represent the health, disease, or treatment status that X-ALD patients may have. In addition to the phenotypic manifestations of the disease, there would be health states for presymptomatic, healthy, bone marrow transplant (a cALD treatment), and death.

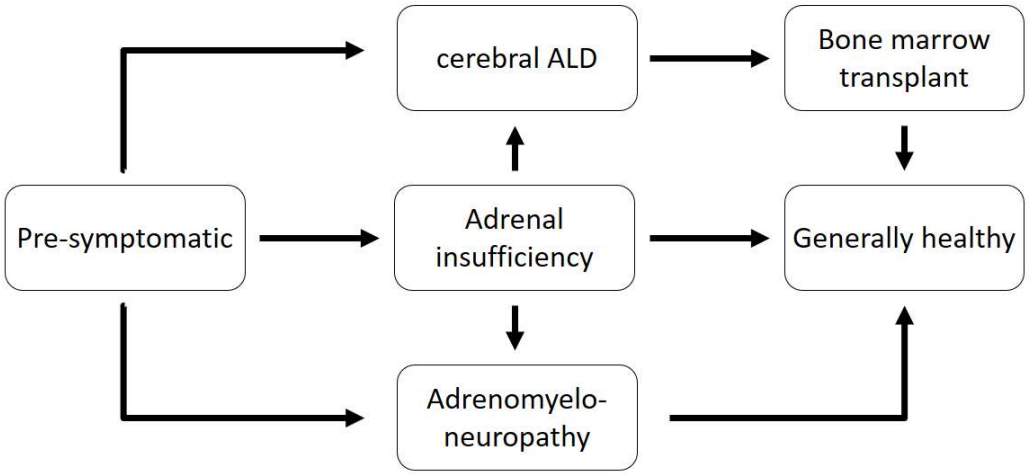
Each health state is also defined by a cost and benefit measure. For cost, we use dollars, and for benefit, we use quality-adjusted-life-years (QALYs). QALYs are a measure of disease burden that reflect both the quality and quantity of life lived.

To begin parsing X-ALD's various options for disease progression, a simplified Markov model was created which assumed that all presymptomatic newborns eventually develop cALD, abnormal adrenal function, or AMN. Both cALD and AMN are also assumed to always include abnormal adrenal function. cALD can be treated with bone marrow transplant while abnormal adrenal function and AMN can be treated with various symptom-specific treatments.

X-ALD Newborn Screening Status, August 2016



X-ALD Newborn Screening *Simplified* Disease State Transition Model



Question and Hypothesis

Is newborn screening for X-linked adrenoleukodystrophy cost-effective?

Preliminary literature review and findings indicate 'Yes.'
To what extent is not clearly known.

Next Steps

1. **Validate proof of concept with simplified Markov model.**
2. **Undergo expert opinion review process to modify and expand Markov model and continually assess validity of model assumptions.**
3. **Share findings with 30+ states that currently have no plans to screen X-ALD.**

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